REMARKS/ARGUMENTS

The Pending Claims

Claims 1-8, 16, 17, and 19-23 currently are pending. The claims are directed to a nutrition trace element composition comprising selenium and zinc, and a method of using the composition.

The Amendments to the Claims

Claims 1 and 16 have been amended to recite that one daily dose of the composition contains 1 mg-2 mg of selenium and 30 mg-100 mg of zinc. Claim 4 has been amended to recite that the composition exists as a concentrate with 1 mg/ml of selenium and 30 mg/ml of zinc. The amendments to claims 1, 4, and 16 are supported by the specification at, e.g., page 12, lines 13-14 and lines 26-28. Claim 23 has been amended to clarify that the composition comprises electrolytes, wherein the electrolytes are in the form of electrolyte concentrates. This amendment is supported by the specification at, e.g., page 1, lines 8-9. No new matter has been added by way of these amendments.

The Office Action

The Office Action rejects claim 23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Office Action rejects claims 1-8, 16, 17, and 19-23 under 35 U.S.C. § 103(a) as allegedly obvious over Frankel ("Supplementation of Trace Elements in Parenteral Nutrition: Rationale and Recommendations"), alone or in combination with Ballevre et al. (U.S. Patent Application Publication 2003/0161863). Reconsideration of these rejections is respectfully requested.

Discussion of Indefiniteness Rejection

Claim 23 is rejected under Section 112, second paragraph, because it is allegedly not clear whether the composition consists only of electrolyte concentrates, and no other elements, or whether the electrolytes present in the composition can only be in the form of a concentrate. Claim 23, as amended, recites that the composition comprises electrolytes, wherein the electrolytes are in the form of electrolyte concentrates. In view of the

amendment to claim 23, Applicants believe that the rejection under Section 112, second paragraph, should be withdrawn.

Discussion of Obviousness Rejection

Claims 1, 8, 16, 17, and 19-23 have been rejected under Section 103(a) as allegedly obvious over Frankel alone or in combination with Ballevre et al. These rejections are traversed for the reasons set forth below.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned Graham factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

Regarding the scope and content of the prior art, Frankel discloses compositions for total parenteral nutrition (TPN) therapy. In particular, Frankel recommends supplementation of chromium, copper, manganese, selenium, and zinc for most patients on TPN therapy. Frankel recommends a "minimum provision" of 50 mcg/day (i.e., 0.05 mg/day) of selenium (Frankel at page 587, fourth paragraph). Frankel recommends a minimum of 5 mg/day of zinc and discloses that as much as 10 mg/day of zinc can be provided. Ballevre et al. discloses an enteral nutrition composition comprising micronutrients, including selenium and zinc, but excluding iron. Specifically, the composition can comprise about 5 mg to about 10 mg zinc, and about 40 μg to about 100 μg (i.e., about 0.04 mg to about 0.1 mg) selenium.

For the sake of argument and for purposes of the present analysis, one of ordinary skill in the art can be assumed to be someone with an advanced degree in a relevant field and a few years of experience in the relevant art.

Claims 1 and 16, as amended, require a nutrition trace element composition which contains 1 mg-2 mg of selenium and 30 mg-100 mg of zinc in one daily dose of the composition. Frankel does not disclose a composition containing zinc in the concentrations currently claimed. Frankel also does not disclose the claimed selenium ranges with sufficient specificity to lead one of ordinary skill in the art to choose the claimed selenium concentrations. In this respect, the minimum dose of 50 mcg/day of selenium disclosed in Frankel is 20 times less than the minimum dose of selenium required by the pending claims. There is no specific teaching or suggestion in Frankel to prepare a composition containing the relatively small range of selenium concentrations as presently claimed.

Ballevre et al. discloses an enteral nutrition composition comprising micronutrients, including selenium and zinc, but excluding iron. Specifically, the composition can comprise about 5 mg to about 10 mg zinc, and about 40 μg to about 100 μg (i.e., about 0.04 mg to about 0.1 mg) selenium. Ballevre et al., however, does not disclose or suggest a composition comprising 1-2 mg of selenium and 30-100 mg of zinc.

Based on the foregoing, the combination of cited references does not disclose or suggest the subject matter of claims 1 and 16. For this reason alone, the subject matter of claims 1 and 16, and claims depending therefrom, is not obvious over the combination of cited references.

Furthermore, and contrary to the assertion of the Office, the claimed invention involves surprising and unexpected results (see Rule 132 Declarations of D. Thomas Stiefel dated December 28, 2009, and August 13, 2010). For example, Applicants have demonstrated that compositions comprising selenium and zinc in the claimed concentrations can be used to successfully treat intensive care patients so that their selenium values and zinc values are maintained at normal levels. These concentrations are well beyond the recommendations in the prior art, as well as the levels in selenium supplement compositions commercially available at the time of the filing of the present application. For example, the claimed selenium and zinc concentrations exceed the tolerable uptake intake levels (UL) for

selenium recommended by the World Health Organization (WHO) (see also, e.g., Food and Nutrition Board of the Institute of Medicine (IOM), ed., *Selenium, In: Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*, National Academy Press (2000), pp. 284-324 (submitted herewith)). Moreover, the claimed selenium and zinc concentrations are in a range in which, prior to the filing of the present application, one of ordinary skill in the art would have assumed that toxic side effects would result. Applicants, however, have demonstrated in clinical trials described in both the application (see, e.g., the Examples) and the Rule 132 declarations that the claimed selenium and zinc concentrations were surprisingly not toxic when administered to intensive care patients and lowered the risk of infection, as compared to patients who were treated with a lower dose of selenium. Accordingly, the surprising finding by Applicants is that the beneficial dose range for selenium and zinc in the treatment of intensive care patients is much higher than the dose ranges recommended in the prior art for intensive care patients (see, e.g., Ballevre et al.). It is also surprising that a selenium dose within the claimed range produces normal levels of selenium in the blood and serum of patients and does not induce toxic side-effects.

The only way in which the combined disclosures of the cited references can be considered as teaching or suggesting the present invention as defined by the pending claims is through the use of hindsight, i.e., with the knowledge of the present application and the invention as claimed therein. It is impermissible for the Patent Office to engage in hindsight reconstruction of the claimed invention by using Applicants' invention as a template and selecting and combining elements from references to fill in that template. See *In re Gorman*, 933 F.2d 982, 18 U.S.P.Q.2d 1885 (Fed. Cir. 1991). As stated by the Federal Circuit: "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'" *Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988), quoting *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012, 217 U.S.P.Q. 193, 199 (Fed. Cir. 1983).

In view of the foregoing, the present invention as defined by the pending claims must be considered unobvious over the combination of the cited references. Accordingly, Applicants request that the rejection under Section 103(a) be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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